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SEQUENCE LISTING

FROM CENTER 1600/2900

<110> Anderson, John P.

Basi, Guriqbal

Doane, Minh Tam

Frigon, Normand

John, Varghese

Power, Michael

Sinha, Sukanto

Tatsuno, Gwen

Tung, Jay

Wang, Shuwen

McConlogue, Lisa

<120> Beta-Secretase Enzyme Compositions and Methods

<130> 228-US-NEW

<140> US 09/471,669

<141> 1999-12-24

<150> 60/114,408

<151> 1998-12-31

<150> 60/119,571

<151> 1999-02-10

<150> 60/139,172

<151> 1999-06-15

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<211> 501

<212> PRT

<213> Homo sapiens

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5


10

15

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 20 25 30  
 Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp ✓  
 35 40 45  
 Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val ✓  
 50 55 60  
 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr ✓  
 65 70 75 80  
 Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser  
 85 90 95  
 Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr ✓  
 100 105 110  
 Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val ✓  
 115 120 125  
 Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp  
 130 135 140  
 Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile  
 145 150 155 160  
 Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp  
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 Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp  
 180 185 190  
 Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro  
 195 200 205  
 Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln  
 210 215 220  
 Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile  
 225 230 235 240  
 Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg  
 245 250 255  
 Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln  
 260 265 270  
 Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val  
 275 280 285  
 Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala  
 290 295 300  
 Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp  
 305 310 315 320



Val  
 codon  
 GTG



Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr  
 325 330 335  
 Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val  
 340 345 350  
 Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg  
 355 360 365  
 Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala  
 370 375 380  
 Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu  
 385 390 395 400  
 Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala  
 405 410 415  
 Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu  
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 Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro  
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 Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala  
 450 455 460  
 Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp  
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<211> 24

<212> DNA

<213> Homo sapiens

<400> 3

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24

<210> 4

<211> 24

<212> DNA

<213> Artificial Sequence

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<223> Degenerate oligonucleotide primer derived from SEQ  
ID NO: 2

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gagagacgar garccwgaag agcc

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<210> 5

<211> 24

<212> DNA

<213> Artificial Sequence

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<223> Degenerate oligonucleotide primer derived from SEQ  
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<213> Artificial Sequence

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<210> 7

<211> 23

<212> DNA

<213> Artificial Sequence

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ID NO: 2

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23

<210> 8

<211> 23

<212> DNA

<213> Artificial Sequence

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<223> Degenerate oligonucleotide primer derived from SEQ

ID NO: 2

<400> 8

agagacgarg arccsgaaga gcc

23

<210> 9

<211> 23

<212> DNA

<213> Artificial Sequence

<220>

<223> Degenerate oligonucleotide primer derived from SEQ

ID NO: 2

<400> 9

agagacgarg arccsgaaga acc

23

<210> 10

<211> 23

<212> DNA

<213> Artificial Sequence

<220>

<223> Degenerate oligonucleotide primer derived from SEQ

ID NO: 2

<400> 10

agagacgarg arccsgagga acc

23

<210> 11

<211> 23

<212> DNA

<213> Artificial Sequence

<220>

<223> Degenerate oligonucleotide primer derived from SEQ  
ID NO: 2

<400> 11

cgtcacagrt trtcaaccat ctc

23

<210> 12

<211> 23

<212> DNA

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ID NO: 2

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cgtcacagrt trtctacat ctc

23

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ID NO: 2

<400> 13

cgtcacagrt trtccacat ctc

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<210> 14

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ID NO: 2

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<210> 15

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<223> Degenerate oligonucleotide primer derived from SEQ

ID NO: 2

<400> 15

cgtcacagrt trtcaaccat ttc

23

<210> 16

<211> 23

<212> DNA

<213> Artificial Sequence

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<223> Degenerate oligonucleotide primer derived from SEQ

ID NO: 2

<400> 16

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<210> 17



<211> 23

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<223> Degenerate oligonucleotide primer derived from SEQ

ID NO: 2

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<210> 18

<211> 23

<212> DNA

<213> Artificial Sequence

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<223> Degenerate oligonucleotide primer derived from SEQ

ID NO: 2

<400> 18

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<210> 19

<211> 20

<212> DNA

<213> Artificial Sequence

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ID NO: 2

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<210> 20

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ID NO: 2

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<211> 24

<212> DNA

<213> Artificial Sequence

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<223> Degenerate oligonucleotide primer derived from SEQ

ID NO: 2

<400> 21

gtgatggcag caatggtggc acgc

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<210> 22

<211> 17

<212> DNA

<213> Artificial Sequence

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<221> misc\_feature

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<223> n = A,T,C or G

<400> 22

gaygargagc cngagga

17

<210> 23

<211> 17

<212> DNA

<213> Artificial Sequence

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<221> misc\_feature

<222> (1)...(17)

<223> n = A,T,C or G

<400> 23

gaygargagc cngaaga

17

<210> 24

<211> 17

<212> DNA

<213> Artificial Sequence

<220>

<223> Degenerate oligonucleotide primer

<221> misc\_feature

<222> (1)...(17)

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<400> 24

gaygargaac cngagga

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<210> 25

<211> 17

<212> DNA

<213> Artificial Sequence

<220>

<223> Degenerate oligonucleotide primer

<221> misc\_feature

<222> (1)...(17)

<223> n = A,T,C or G

<400> 25

gaygargaac cngaaga

17

<210> 26

<211> 15

<212> DNA

<213> Artificial Sequence

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<223> Degenerate oligonucleotide primer

<221> misc\_feature

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<210> 27

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<210> 28

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<222> (1)...(17)

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<223> Degenerate oligonucleotide primer

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<210> 31

<211> 27

<212> DNA

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<223> Degenerate oligonucleotide primer

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<223> Degenerate oligonucleotide primer

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atattctaga gaygargagc ccgaaga

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<210> 33

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<210> 34

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<223> Degenerate oligonucleotide primer

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<223> Degenerate oligonucleotide primer

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<210> 42

<211> 2348

<212> DNA

<213> Homo sapiens

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<212> PRT

<213> Homo sapiens

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Glu	Met	Thr	Val	Gly	Ser	Pro	Pro	Gln	Thr	Leu	Asn	Ile	Leu	Val	Asp
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Thr	Gly	Ser	Ser	Asn	Phe	Ala	Val	Gly	Ala	Ala	Pro	His	Pro	Phe	Leu
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His	Arg	Tyr	Tyr	Gln	Arg	Gln	Leu	Ser	Ser	Thr	Tyr	Arg	Asp	Leu	Arg
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Lys	Gly	Val	Tyr	Val	Pro	Tyr	Thr	Gln	Gly	Lys	Trp	Glu	Gly	Glu	Leu
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Gly	Thr	Asp	Leu	Val	Ser	Ile	Pro	His	Gly	Pro	Asn	Val	Thr	Val	Arg
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Ala	Asn	Ile	Ala	Ala	Ile	Thr	Glu	Ser	Asp	Lys	Phe	Phe	Ile	Asn	Gly
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Ser	Asn	Trp	Glu	Gly	Ile	Leu	Gly	Leu	Ala	Tyr	Ala	Glu	Ile	Ala	Arg
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Phe	Glu	Ala	Ala	Val	Lys	Ser	Ile	Lys	Ala	Ala	Ser	Ser	Thr	Glu	Lys
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Phe	Pro	Asp	Gly	Phe	Trp	Leu	Gly	Glu	Gln	Leu	Val	Cys	Trp	Gln	Ala
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Gly	Thr	Thr	Pro	Trp	Asn	Ile	Phe	Pro	Val	Ile	Ser	Leu	Tyr	Leu	Met
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 Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr  
 325 330 335  
 Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val  
 340 345 350  
 Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile  
 355 360 365  
 Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala  
 370 375 380  
 Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr  
 385 390 395 400  
 Asn Ile Pro Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val  
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<210> 44

<211> 2348

<212> DNA

<213> Homo sapiens

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<223> Flag sequence

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<210> 46

<211> 22

<212> PRT

<213> Homo sapiens

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<210> 47

<211> 23

<212> PRT

<213> Homo sapiens

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Leu Gly Leu Arg Leu Pro Arg

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<212> PRT

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<223> Synthetic oligopeptide substrate

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Ser Glu Val Asn Leu Asp Ala Glu Phe

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<213> Artificial Sequence

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<223> Synthetic oligopeptide substrate

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<220>

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<213> Homo sapiens

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 Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp  
 35 40 45  
 Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val  
 50 55 60  
 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr  
 65 70 75 80  
 Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser  
 85 90 95  
 Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr  
 100 105 110  
 Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val  
 115 120 125  
 Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp  
 130 135 140



Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile  
 145 150 155 160  
 Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp  
 165 170 175  
 Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp  
 180 185 190  
 Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro  
 195 200 205  
 Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln  
 210 215 220  
 Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile  
 225 230 235 240  
 Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg  
 245 250 255  
 Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln  
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 Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val  
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 Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val  
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 Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala  
 370 375 380  
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 Val Ser Ala

<210> 58

<211> 407

<212> PRT

<213> Homo sapiens

<400> 58

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Glu	Met	Thr	Val	Gly	Ser	Pro	Pro	Gln	Thr	Leu	Asn	Ile	Leu	Val	Asp
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Thr	Gly	Ser	Ser	Asn	Phe	Ala	Val	Gly	Ala	Ala	Pro	His	Pro	Phe	Leu
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His	Arg	Tyr	Tyr	Gln	Arg	Gln	Leu	Ser	Ser	Thr	Tyr	Arg	Asp	Leu	Arg
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Lys	Gly	Val	Tyr	Val	Pro	Tyr	Thr	Gln	Gly	Lys	Trp	Glu	Gly	Glu	Leu
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Gly	Thr	Asp	Leu	Val	Ser	Ile	Pro	His	Gly	Pro	Asn	Val	Thr	Val	Arg
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Ala	Asn	Ile	Ala	Ala	Ile	Thr	Glu	Ser	Asp	Lys	Phe	Phe	Ile	Asn	Gly
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Ser	Asn	Trp	Glu	Gly	Ile	Leu	Gly	Leu	Ala	Tyr	Ala	Glu	Ile	Ala	Arg
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Pro	Asp	Asp	Ser	Leu	Glu	Pro	Phe	Phe	Asp	Ser	Leu	Val	Lys	Gln	Thr
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Leu	Asn	Gln	Ser	Glu	Val	Leu	Ala	Ser	Val	Gly	Gly	Ser	Met	Ile	Ile
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Gly	Gly	Ile	Asp	His	Ser	Leu	Tyr	Thr	Gly	Ser	Leu	Trp	Tyr	Thr	Pro
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Ser	Ile	Val	Asp	Ser	Gly	Thr	Thr	Asn	Leu	Arg	Leu	Pro	Lys	Lys	Val
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Phe	Glu	Ala	Ala	Val	Lys	Ser	Ile	Lys	Ala	Ala	Ser	Ser	Thr	Glu	Lys

260	265	270
Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala		
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Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met		
290	295	300
Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln		
305	310	315
Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr		
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Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val		
340	345	350
Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile		
355	360	365
Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala		
370	375	380
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<210> 59

<211> 452

<212> PRT

<213> Homo sapiens

<400> 59

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Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp		
35	40	45
Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val		
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Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr		
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Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser		
85	90	95

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 165 170 175  
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 180 185 190  
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 225 230 235 240  
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 245 250 255  
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 275 280 285  
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 355 360 365  
 Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala  
 370 375 380  
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 385 390 395 400

Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala  
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                     420                    425                    430  
 Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro  
                     435                    440                    445  
 Gln Thr Asp Glu  
                     450

<210> 60

<211> 420

<212> PRT

<213> Homo sapiens

<400> 60

Met Ala Gln Ala Leu Pro Trp Leu Leu Leu Trp Met Gly Ala Gly Val  
 1                    5                    10                    15  
 Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser  
                     20                    25                    30  
 Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp  
                     35                    40                    45  
 Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val  
                     50                    55                    60  
 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr  
 65                    70                    75                    80  
 Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser  
                     85                    90                    95  
 Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr  
                     100                    105                    110  
 Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val  
                     115                    120                    125  
 Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp  
                     130                    135                    140  
 Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile  
 145                    150                    155                    160  
 Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp  
                     165                    170                    175  
 Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp

	180		185		190										
Ser	Leu	Glu	Pro	Phe	Phe	Asp	Ser	Leu	Val	Lys	Gln	Thr	His	Val	Pro
	195						200				205				
Asn	Leu	Phe	Ser	Leu	Gln	Leu	Cys	Gly	Ala	Gly	Phe	Pro	Leu	Asn	Gln
	210					215					220				
Ser	Glu	Val	Leu	Ala	Ser	Val	Gly	Gly	Ser	Met	Ile	Ile	Gly	Gly	Ile
225					230					235					240
Asp	His	Ser	Leu	Tyr	Thr	Gly	Ser	Leu	Trp	Tyr	Thr	Pro	Ile	Arg	Arg
				245					250				255		
Glu	Trp	Tyr	Tyr	Glu	Val	Ile	Ile	Val	Arg	Val	Glu	Ile	Asn	Gly	Gln
			260					265				270			
Asp	Leu	Lys	Met	Asp	Cys	Lys	Glu	Tyr	Asn	Tyr	Asp	Lys	Ser	Ile	Val
	275						280				285				
Asp	Ser	Gly	Thr	Thr	Asn	Leu	Arg	Leu	Pro	Lys	Lys	Val	Phe	Glu	Ala
	290				295					300					
Ala	Val	Lys	Ser	Ile	Lys	Ala	Ala	Ser	Ser	Thr	Glu	Lys	Phe	Pro	Asp
305				310					315					320	
Gly	Phe	Trp	Leu	Gly	Glu	Gln	Leu	Val	Cys	Trp	Gln	Ala	Gly	Thr	Thr
			325					330				335			
Pro	Trp	Asn	Ile	Phe	Pro	Val	Ile	Ser	Leu	Tyr	Leu	Met	Gly	Glu	Val
		340				345				350					
Thr	Asn	Gln	Ser	Phe	Arg	Ile	Thr	Ile	Leu	Pro	Gln	Gln	Tyr	Leu	Arg
	355				360				365						
Pro	Val	Glu	Asp	Val	Ala	Thr	Ser	Gln	Asp	Asp	Cys	Tyr	Lys	Phe	Ala
	370				375				380						
Ile	Ser	Gln	Ser	Ser	Thr	Gly	Thr	Val	Met	Gly	Ala	Val	Ile	Met	Glu
385			390					395					400		
Gly	Phe	Tyr	Val	Val	Phe	Asp	Arg	Ala	Arg	Lys	Arg	Ile	Gly	Phe	Ala
			405					410				415			
Val	Ser	Ala	Cys												
	420														

<210> 61

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic peptide inhibitor

<221> MOD\_RES

<222> 4

<223> Xaa = hydroxyethylene

<400> 61

Glu Val Met Xaa Val Ala Glu Phe

1 5

<210> 62

<211> 26

<212> PRT

<213> Homo sapiens

<400> 62

Leu Met Thr Ile Ala Tyr Val Met Ala Ala Ile Cys Ala Leu Phe Met

1 5 10 15

Leu Pro Leu Cys Leu Met Val Cys Gln Trp

20 25

<210> 63

<211> 33

<212> PRT

<213> Homo sapiens

<220>

<223> P26-P4'sw peptide substrate

<400> 63

Cys Gly Gly Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser Gly Leu

1 5 10 15

Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Asn Leu Asp Ala Glu

20 25 30

Phe

<210> 64

<211> 29

<212> PRT

<213> Homo sapiens

<220>

<223> P26-P1' peptide substrate with CGG linker

<400> 64

Cys Gly Gly Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser Gly Leu  
1 5 10 15  
Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Asn Leu  
20 25

<210> 65

<211> 501

<212> PRT

<213> Mus musculus

<400> 65

Met Ala Pro Ala Leu His Trp Leu Leu Leu Trp Val Gly Ser Gly Met  
1 5 10 15  
Leu Pro Ala Gln Gly Thr His Leu Gly Ile Arg Leu Pro Leu Arg Ser  
20 25 30  
Gly Leu Ala Gly Pro Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp  
35 40 45  
Glu Glu Ser Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val  
50 55 60  
Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr  
65 70 75 80  
Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser  
85 90 95  
Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr  
100 105 110  
Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val  
115 120 125  
Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp  
130 135 140  
Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile



145		150		155		160									
Ala	Ala	Ile	Thr	Glu	Ser	Asp	Lys	Phe	Phe	Ile	Asn	Gly	Ser	Asn	Trp
				165						170				175	
Glu	Gly	Ile	Leu	Gly	Leu	Ala	Tyr	Ala	Glu	Ile	Ala	Arg	Pro	Asp	Asp
				180						185				190	
Ser	Leu	Glu	Pro	Phe	Phe	Asp	Ser	Leu	Val	Lys	Gln	Thr	His	Ile	Pro
				195				200					205		
Asn	Ile	Phe	Ser	Leu	Gln	Leu	Cys	Gly	Ala	Gly	Phe	Pro	Leu	Asn	Gln
				210				215				220			
Thr	Glu	Ala	Leu	Ala	Ser	Val	Gly	Gly	Ser	Met	Ile	Ile	Gly	Gly	Ile
225					230					235				240	
Asp	His	Ser	Leu	Tyr	Thr	Gly	Ser	Leu	Trp	Tyr	Thr	Pro	Ile	Arg	Arg
				245					250				255		
Glu	Trp	Tyr	Tyr	Glu	Val	Ile	Ile	Val	Arg	Val	Glu	Ile	Asn	Gly	Gln
				260				265				270			
Asp	Leu	Lys	Met	Asp	Cys	Lys	Glu	Tyr	Asn	Tyr	Asp	Lys	Ser	Ile	Val
				275				280				285			
Asp	Ser	Gly	Thr	Thr	Asn	Leu	Arg	Leu	Pro	Lys	Lys	Val	Phe	Glu	Ala
				290				295				300			
Ala	Val	Lys	Ser	Ile	Lys	Ala	Ala	Ser	Ser	Thr	Glu	Lys	Phe	Pro	Asp
305					310					315				320	
Gly	Phe	Trp	Leu	Gly	Glu	Gln	Leu	Val	Cys	Trp	Gln	Ala	Gly	Thr	Thr
				325					330				335		
Pro	Trp	Asn	Ile	Phe	Pro	Val	Ile	Ser	Leu	Tyr	Leu	Met	Gly	Glu	Val
				340				345				350			
Thr	Asn	Gln	Ser	Phe	Arg	Ile	Thr	Ile	Leu	Pro	Gln	Gln	Tyr	Leu	Arg
				355				360				365			
Pro	Val	Glu	Asp	Val	Ala	Thr	Ser	Gln	Asp	Asp	Cys	Tyr	Lys	Phe	Ala
				370				375			380				
Val	Ser	Gln	Ser	Ser	Thr	Gly	Thr	Val	Met	Gly	Ala	Val	Ile	Met	Glu
385					390					395				400	
Gly	Phe	Tyr	Val	Val	Phe	Asp	Arg	Ala	Arg	Lys	Arg	Ile	Gly	Phe	Ala
				405					410				415		
Val	Ser	Ala	Cys	His	Val	His	Asp	Glu	Phe	Arg	Thr	Ala	Ala	Val	Glu
				420				425				430			
Gly	Pro	Phe	Val	Thr	Ala	Asp	Met	Glu	Asp	Cys	Gly	Tyr	Asn	Ile	Pro
				435				440				445			
Gln	Thr	Asp	Glu	Ser	Thr	Leu	Met	Thr	Ile	Ala	Tyr	Val	Met	Ala	Ala

450                      455                      460  
 Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp  
 465                      470                      475                      480  
 Arg Cys Leu Arg Cys Leu Arg His Gln His Asp Asp Phe Gly Asp Asp  
                          485                      490                      495  
 Ile Ser Leu Leu Lys  
                          500

<210> 66

<211> 480

<212> PRT

<213> Homo sapiens

<400> 66

Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser Gly Leu Gly Gly Ala  
 1                      5                      10                      15  
 Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp Glu Glu Pro Glu Glu  
                          20                      25                      30  
 Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly  
                          35                      40                      45  
 Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro  
                          50                      55                      60  
 Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val  
 65                      70                      75                      80  
 Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu  
                          85                      90                      95  
 Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr  
                          100                      105                      110  
 Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro  
                          115                      120                      125  
 His Gly Pro Asn Val Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu  
                          130                      135                      140  
 Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly  
 145                      150                      155                      160  
 Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe  
                          165                      170                      175  
 Phe Asp Ser Leu Val Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu  
                          180                      185                      190

Gln	Leu	Cys	Gly	Ala	Gly	Phe	Pro	Leu	Asn	Gln	Ser	Glu	Val	Leu	Ala			
		195					200					205						
Ser	Val	Gly	Gly	Ser	Met	Ile	Ile	Gly	Gly	Ile	Asp	His	Ser	Leu	Tyr			
		210				215					220							
Thr	Gly	Ser	Leu	Trp	Tyr	Thr	Pro	Ile	Arg	Arg	Glu	Trp	Tyr	Tyr	Glu			
225					230				235						240			
Val	Ile	Ile	Val	Arg	Val	Glu	Ile	Asn	Gly	Gln	Asp	Leu	Lys	Met	Asp			
				245				250					255					
Cys	Lys	Glu	Tyr	Asn	Tyr	Asp	Lys	Ser	Ile	Val	Asp	Ser	Gly	Thr	Thr			
			260					265					270					
Asn	Leu	Arg	Leu	Pro	Lys	Lys	Val	Phe	Glu	Ala	Ala	Val	Lys	Ser	Ile			
		275				280						285						
Lys	Ala	Ala	Ser	Ser	Thr	Glu	Lys	Phe	Pro	Asp	Gly	Phe	Trp	Leu	Gly			
		290				295					300							
Glu	Gln	Leu	Val	Cys	Trp	Gln	Ala	Gly	Thr	Thr	Pro	Trp	Asn	Ile	Phe			
305				310					315					320				
Pro	Val	Ile	Ser	Leu	Tyr	Leu	Met	Gly	Glu	Val	Thr	Asn	Gln	Ser	Phe			
				325				330					335					
Arg	Ile	Thr	Ile	Leu	Pro	Gln	Gln	Tyr	Leu	Arg	Pro	Val	Glu	Asp	Val			
		340				345						350						
Ala	Thr	Ser	Gln	Asp	Asp	Cys	Tyr	Lys	Phe	Ala	Ile	Ser	Gln	Ser	Ser			
		355				360						365						
Thr	Gly	Thr	Val	Met	Gly	Ala	Val	Ile	Met	Glu	Gly	Phe	Tyr	Val	Val			
		370			375					380								
Phe	Asp	Arg	Ala	Arg	Lys	Arg	Ile	Gly	Phe	Ala	Val	Ser	Ala	Cys	His			
385				390					395					400				
Val	His	Asp	Glu	Phe	Arg	Thr	Ala	Ala	Val	Glu	Gly	Pro	Phe	Val	Thr			
			405					410					415					
Leu	Asp	Met	Glu	Asp	Cys	Gly	Tyr	Asn	Ile	Pro	Gln	Thr	Asp	Glu	Ser			
		420						425				430						
Thr	Leu	Met	Thr	Ile	Ala	Tyr	Val	Met	Ala	Ala	Ile	Cys	Ala	Leu	Phe			
		435				440						445						
Met	Leu	Pro	Leu	Cys	Leu	Met	Val	Cys	Gln	Trp	Arg	Cys	Leu	Arg	Cys			
		450				455					460							
Leu	Arg	Gln	Gln	His	Asp	Asp	Phe	Ala	Asp	Asp	Ile	Ser	Leu	Leu	Lys			
465				470					475					480				

<210> 67

<211> 444

<212> PRT

<213> Homo sapiens

<400> 67

Gly	Ser	Phe	Val	Glu	Met	Val	Asp	Asn	Leu	Arg	Gly	Lys	Ser	Gly	Gln
1				5					10					15	
Gly	Tyr	Tyr	Val	Glu	Met	Thr	Val	Gly	Ser	Pro	Pro	Gln	Thr	Leu	Asn
			20					25					30		
Ile	Leu	Val	Asp	Thr	Gly	Ser	Ser	Asn	Phe	Ala	Val	Gly	Ala	Ala	Pro
		35					40					45			
His	Pro	Phe	Leu	His	Arg	Tyr	Tyr	Gln	Arg	Gln	Leu	Ser	Ser	Thr	Tyr
	50					55				60					
Arg	Asp	Leu	Arg	Lys	Gly	Val	Tyr	Val	Pro	Tyr	Thr	Gln	Gly	Lys	Trp
65					70					75				80	
Glu	Gly	Glu	Leu	Gly	Thr	Asp	Leu	Val	Ser	Ile	Pro	His	Gly	Pro	Asn
			85						90					95	
Val	Thr	Val	Arg	Ala	Asn	Ile	Ala	Ala	Ile	Thr	Glu	Ser	Asp	Lys	Phe
		100						105					110		
Phe	Ile	Asn	Gly	Ser	Asn	Trp	Glu	Gly	Ile	Leu	Gly	Leu	Ala	Tyr	Ala
	115						120					125			
Glu	Ile	Ala	Arg	Pro	Asp	Asp	Ser	Leu	Glu	Pro	Phe	Phe	Asp	Ser	Leu
	130					135					140				
Val	Lys	Gln	Thr	His	Val	Pro	Asn	Leu	Phe	Ser	Leu	Gln	Leu	Cys	Gly
145				150					155					160	
Ala	Gly	Phe	Pro	Leu	Asn	Gln	Ser	Glu	Val	Leu	Ala	Ser	Val	Gly	Gly
		165						170					175		
Ser	Met	Ile	Ile	Gly	Gly	Ile	Asp	His	Ser	Leu	Tyr	Thr	Gly	Ser	Leu
		180					185						190		
Trp	Tyr	Thr	Pro	Ile	Arg	Arg	Glu	Trp	Tyr	Tyr	Glu	Val	Ile	Ile	Val
	195					200						205			
Arg	Val	Glu	Ile	Asn	Gly	Gln	Asp	Leu	Lys	Met	Asp	Cys	Lys	Glu	Tyr
	210				215					220					
Asn	Tyr	Asp	Lys	Ser	Ile	Val	Asp	Ser	Gly	Thr	Thr	Asn	Leu	Arg	Leu
225				230					235					240	
Pro	Lys	Lys	Val	Phe	Glu	Ala	Ala	Val	Lys	Ser	Ile	Lys	Ala	Ala	Ser
		245						250					255		
Ser	Thr	Glu	Lys	Phe	Pro	Asp	Gly	Phe	Trp	Leu	Gly	Glu	Gln	Leu	Val

	260		265		270										
Cys	Trp	Gln	Ala	Gly	Thr	Thr	Pro	Trp	Asn	Ile	Phe	Pro	Val	Ile	Ser
	275						280					285			
Leu	Tyr	Leu	Met	Gly	Glu	Val	Thr	Asn	Gln	Ser	Phe	Arg	Ile	Thr	Ile
	290						295					300			
Leu	Pro	Gln	Gln	Tyr	Leu	Arg	Pro	Val	Glu	Asp	Val	Ala	Thr	Ser	Gln
305						310				315					320
Asp	Asp	Cys	Tyr	Lys	Phe	Ala	Ile	Ser	Gln	Ser	Ser	Thr	Gly	Thr	Val
				325					330					335	
Met	Gly	Ala	Val	Ile	Met	Glu	Gly	Phe	Tyr	Val	Val	Phe	Asp	Arg	Ala
			340					345					350		
Arg	Lys	Arg	Ile	Gly	Phe	Ala	Val	Ser	Ala	Cys	His	Val	His	Asp	Glu
	355						360					365			
Phe	Arg	Thr	Ala	Ala	Val	Glu	Gly	Pro	Phe	Val	Thr	Leu	Asp	Met	Glu
	370					375					380				
Asp	Cys	Gly	Tyr	Asn	Ile	Pro	Gln	Thr	Asp	Glu	Ser	Thr	Leu	Met	Thr
385				390					395						400
Ile	Ala	Tyr	Val	Met	Ala	Ala	Ile	Cys	Ala	Leu	Phe	Met	Leu	Pro	Leu
			405						410				415		
Cys	Leu	Met	Val	Cys	Gln	Trp	Arg	Cys	Leu	Arg	Cys	Leu	Arg	Gln	Gln
		420					425					430			
His	Asp	Asp	Phe	Ala	Asp	Asp	Ile	Ser	Leu	Leu	Lys				
	435						440								

<210> 68

<211> 395

<212> PRT

<213> Homo sapiens

<400> 68

Gly	Ser	Phe	Val	Glu	Met	Val	Asp	Asn	Leu	Arg	Gly	Lys	Ser	Gly	Gln
1				5					10					15	
Gly	Tyr	Tyr	Val	Glu	Met	Thr	Val	Gly	Ser	Pro	Pro	Gln	Thr	Leu	Asn
			20					25					30		
Ile	Leu	Val	Asp	Thr	Gly	Ser	Ser	Asn	Phe	Ala	Val	Gly	Ala	Ala	Pro
		35					40					45			
His	Pro	Phe	Leu	His	Arg	Tyr	Tyr	Gln	Arg	Gln	Leu	Ser	Ser	Thr	Tyr
	50						55					60			

Arg	Asp	Leu	Arg	Lys	Gly	Val	Tyr	Val	Pro	Tyr	Thr	Gln	Gly	Lys	Trp
65					70					75					80
Glu	Gly	Glu	Leu	Gly	Thr	Asp	Leu	Val	Ser	Ile	Pro	His	Gly	Pro	Asn
				85					90					95	
Val	Thr	Val	Arg	Ala	Asn	Ile	Ala	Ala	Ile	Thr	Glu	Ser	Asp	Lys	Phe
			100					105					110		
Phe	Ile	Asn	Gly	Ser	Asn	Trp	Glu	Gly	Ile	Leu	Gly	Leu	Ala	Tyr	Ala
		115					120					125			
Glu	Ile	Ala	Arg	Pro	Asp	Asp	Ser	Leu	Glu	Pro	Phe	Phe	Asp	Ser	Leu
	130					135					140				
Val	Lys	Gln	Thr	His	Val	Pro	Asn	Leu	Phe	Ser	Leu	Gln	Leu	Cys	Gly
145					150					155					160
Ala	Gly	Phe	Pro	Leu	Asn	Gln	Ser	Glu	Val	Leu	Ala	Ser	Val	Gly	Gly
				165					170					175	
Ser	Met	Ile	Ile	Gly	Gly	Ile	Asp	His	Ser	Leu	Tyr	Thr	Gly	Ser	Leu
			180					185					190		
Trp	Tyr	Thr	Pro	Ile	Arg	Arg	Glu	Trp	Tyr	Tyr	Glu	Val	Ile	Ile	Val
	195						200					205			
Arg	Val	Glu	Ile	Asn	Gly	Gln	Asp	Leu	Lys	Met	Asp	Cys	Lys	Glu	Tyr
	210					215					220				
Asn	Tyr	Asp	Lys	Ser	Ile	Val	Asp	Ser	Gly	Thr	Thr	Asn	Leu	Arg	Leu
225					230					235				240	
Pro	Lys	Lys	Val	Phe	Glu	Ala	Ala	Val	Lys	Ser	Ile	Lys	Ala	Ala	Ser
				245					250					255	
Ser	Thr	Glu	Lys	Phe	Pro	Asp	Gly	Phe	Trp	Leu	Gly	Glu	Gln	Leu	Val
		260						265					270		
Cys	Trp	Gln	Ala	Gly	Thr	Thr	Pro	Trp	Asn	Ile	Phe	Pro	Val	Ile	Ser
	275						280				285				
Leu	Tyr	Leu	Met	Gly	Glu	Val	Thr	Asn	Gln	Ser	Phe	Arg	Ile	Thr	Ile
	290					295					300				
Leu	Pro	Gln	Gln	Tyr	Leu	Arg	Pro	Val	Glu	Asp	Val	Ala	Thr	Ser	Gln
305					310					315					320
Asp	Asp	Cys	Tyr	Lys	Phe	Ala	Ile	Ser	Gln	Ser	Ser	Thr	Gly	Thr	Val
				325					330					335	
Met	Gly	Ala	Val	Ile	Met	Glu	Gly	Phe	Tyr	Val	Val	Phe	Asp	Arg	Ala
			340					345					350		
Arg	Lys	Arg	Ile	Gly	Phe	Ala	Val	Ser	Ala	Cys	His	Val	His	Asp	Glu
		355					360						365		

Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu  
 370 375 380  
 Asp Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu  
 385 390 395

<210> 69

<211> 439

<212> PRT

<213> Homo sapiens

<400> 69

Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu  
 1 5 10 15  
 Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr  
 20 25 30  
 Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His  
 35 40 45  
 Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys  
 50 55 60  
 Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly  
 65 70 75 80  
 Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala  
 85 90 95  
 Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser  
 100 105 110  
 Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro  
 115 120 125  
 Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His  
 130 135 140  
 Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu  
 145 150 155 160  
 Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly  
 165 170 175  
 Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile  
 180 185 190  
 Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn  
 195 200 205  
 Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser

210	215	220													
Ile	Val	Asp	Ser	Gly	Thr	Thr	Asn	Leu	Arg	Leu	Pro	Lys	Lys	Val	Phe
225					230					235				240	
Glu	Ala	Ala	Val	Lys	Ser	Ile	Lys	Ala	Ala	Ser	Ser	Thr	Glu	Lys	Phe
				245					250					255	
Pro	Asp	Gly	Phe	Trp	Leu	Gly	Glu	Gln	Leu	Val	Cys	Trp	Gln	Ala	Gly
			260					265					270		
Thr	Thr	Pro	Trp	Asn	Ile	Phe	Pro	Val	Ile	Ser	Leu	Tyr	Leu	Met	Gly
		275					280					285			
Glu	Val	Thr	Asn	Gln	Ser	Phe	Arg	Ile	Thr	Ile	Leu	Pro	Gln	Gln	Tyr
	290					295				300					
Leu	Arg	Pro	Val	Glu	Asp	Val	Ala	Thr	Ser	Gln	Asp	Asp	Cys	Tyr	Lys
305					310					315				320	
Phe	Ala	Ile	Ser	Gln	Ser	Ser	Thr	Gly	Thr	Val	Met	Gly	Ala	Val	Ile
				325					330				335		
Met	Glu	Gly	Phe	Tyr	Val	Val	Phe	Asp	Arg	Ala	Arg	Lys	Arg	Ile	Gly
		340						345				350			
Phe	Ala	Val	Ser	Ala	Cys	His	Val	His	Asp	Glu	Phe	Arg	Thr	Ala	Ala
	355						360					365			
Val	Glu	Gly	Pro	Phe	Val	Thr	Leu	Asp	Met	Glu	Asp	Cys	Gly	Tyr	Asn
	370					375						380			
Ile	Pro	Gln	Thr	Asp	Glu	Ser	Thr	Leu	Met	Thr	Ile	Ala	Tyr	Val	Met
385					390					395				400	
Ala	Ala	Ile	Cys	Ala	Leu	Phe	Met	Leu	Pro	Leu	Cys	Leu	Met	Val	Cys
				405					410				415		
Gln	Trp	Arg	Cys	Leu	Arg	Cys	Leu	Arg	Gln	Gln	His	Asp	Asp	Phe	Ala
		420						425				430			
Asp	Asp	Ile	Ser	Leu	Leu	Lys									
	435														

<210> 70

<211> 390

<212> PRT

<213> Homo sapiens

<400> 70

Met	Val	Asp	Asn	Leu	Arg	Gly	Lys	Ser	Gly	Gln	Gly	Tyr	Tyr	Val	Glu
1				5					10					15	





Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile  
                           325                          330                          335  
 Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly  
                           340                          345                          350  
 Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala  
                           355                          360                          365  
 Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn  
                           370                          375                          380  
 Ile Pro Gln Thr Asp Glu  
 385                          390

<210> 71

<211> 374

<212> PRT

<213> Homo sapiens

<400> 71

Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val  
   1                          5                          10                          15  
 Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val  
                           20                          25                          30  
 Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp  
                           35                          40                          45  
 Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu  
                           50                          55                          60  
 His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg  
   65                          70                          75                          80  
 Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu  
                           85                          90                          95  
 Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg  
                           100                          105                          110  
 Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly  
                           115                          120                          125  
 Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg  
                           130                          135                          140  
 Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr  
   145                          150                          155                          160  
 His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro

165	170	175
Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile		
180	185	190
Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro		
195	200	205
Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile		
210	215	220
Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys		
225	230	235
Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val		
245	250	255
Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys		
260	265	270
Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala		
275	280	285
Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met		
290	295	300
Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln		
305	310	315
Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr		
325	330	335
Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val		
340	345	350
Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile		
355	360	365
Gly Phe Ala Val Ser Ala		
370		

<210> 72

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> P10-P4'staD-V peptide inhibitor

<221> MOD\_RES

<222> 10

<223> Xaa is statine moiety

<400> 72

Lys Thr Glu Glu Ile Ser Glu Val Asn Xaa Val Ala Glu Phe

1 5 10

<210> 73

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> P4-P4'staD-V peptide inhibitor

<221> MOD\_RES

<222> 5

<223> Xaa is statine moiety

<400> 73

Ser Glu Val Asn Xaa Val Ala Glu Phe

1 5

<210> 74

<211> 431

<212> PRT

<213> Homo sapiens

<400> 74

Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser Gly Leu Gly Gly Ala

1 5 10 15

Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp Glu Glu Pro Glu Glu

20 25 30

Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly

35 40 45

Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro

50 55 60

Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val

65 70 75 80

Gly	Ala	Ala	Pro	His	Pro	Phe	Leu	His	Arg	Tyr	Tyr	Gln	Arg	Gln	Leu			
				85					90					95				
Ser	Ser	Thr	Tyr	Arg	Asp	Leu	Arg	Lys	Gly	Val	Tyr	Val	Pro	Tyr	Thr			
			100					105					110					
Gln	Gly	Lys	Trp	Glu	Gly	Glu	Leu	Gly	Thr	Asp	Leu	Val	Ser	Ile	Pro			
		115					120					125						
His	Gly	Pro	Asn	Val	Thr	Val	Arg	Ala	Asn	Ile	Ala	Ala	Ile	Thr	Glu			
		130					135				140							
Ser	Asp	Lys	Phe	Phe	Ile	Asn	Gly	Ser	Asn	Trp	Glu	Gly	Ile	Leu	Gly			
145					150				155					160				
Leu	Ala	Tyr	Ala	Glu	Ile	Ala	Arg	Pro	Asp	Asp	Ser	Leu	Glu	Pro	Phe			
				165				170					175					
Phe	Asp	Ser	Leu	Val	Lys	Gln	Thr	His	Val	Pro	Asn	Leu	Phe	Ser	Leu			
		180					185					190						
Gln	Leu	Cys	Gly	Ala	Gly	Phe	Pro	Leu	Asn	Gln	Ser	Glu	Val	Leu	Ala			
		195					200					205						
Ser	Val	Gly	Gly	Ser	Met	Ile	Ile	Gly	Gly	Ile	Asp	His	Ser	Leu	Tyr			
	210					215				220								
Thr	Gly	Ser	Leu	Trp	Tyr	Thr	Pro	Ile	Arg	Arg	Glu	Trp	Tyr	Tyr	Glu			
225				230					235					240				
Val	Ile	Ile	Val	Arg	Val	Glu	Ile	Asn	Gly	Gln	Asp	Leu	Lys	Met	Asp			
			245					250					255					
Cys	Lys	Glu	Tyr	Asn	Tyr	Asp	Lys	Ser	Ile	Val	Asp	Ser	Gly	Thr	Thr			
		260					265					270						
Asn	Leu	Arg	Leu	Pro	Lys	Lys	Val	Phe	Glu	Ala	Ala	Val	Lys	Ser	Ile			
		275					280					285						
Lys	Ala	Ala	Ser	Ser	Thr	Glu	Lys	Phe	Pro	Asp	Gly	Phe	Trp	Leu	Gly			
	290					295				300								
Glu	Gln	Leu	Val	Cys	Trp	Gln	Ala	Gly	Thr	Thr	Pro	Trp	Asn	Ile	Phe			
305				310				315					320					
Pro	Val	Ile	Ser	Leu	Tyr	Leu	Met	Gly	Glu	Val	Thr	Asn	Gln	Ser	Phe			
			325					330					335					
Arg	Ile	Thr	Ile	Leu	Pro	Gln	Gln	Tyr	Leu	Arg	Pro	Val	Glu	Asp	Val			
		340					345					350						
Ala	Thr	Ser	Gln	Asp	Asp	Cys	Tyr	Lys	Phe	Ala	Ile	Ser	Gln	Ser	Ser			
		355				360						365						
Thr	Gly	Thr	Val	Met	Gly	Ala	Val	Ile	Met	Glu	Gly	Phe	Tyr	Val	Val			
	370					375				380								



195	200	205
Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser		
210	215	220
Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe		
225	230	235
Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe		
245	250	255
Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly		
260	265	270
Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly		
275	280	285
Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr		
290	295	300
Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys		
305	310	315
Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile		
325	330	335
Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly		
340	345	350
Phe Ala Val Ser Ala Cys His Val His		
355	360	

<210> 76

<211> 63

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(63)

<223> n = A,T,C or G

<400> 76

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aay	63

<210> 77

<211> 21

<212> PRT

<213> Homo sapiens

<400> 77

Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val  
1 5 10 15  
Glu Met Val Asp Asn  
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<210> 78

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Peptide inhibitor P3-P4' XD-V

<221> MOD\_RES

<222> 3

<223> Xaa is hydroxyethylene or statine

<400> 78

Val Met Xaa Val Ala Glu Phe  
1 5

<210> 79

<211> 11

<212> PRT

<213> Homo sapiens

<400> 79

Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val  
1 5 10

<210> 80

<211> 419

<212> DNA

<213> Artificial Sequence



<220>

<223> nucleotide insert in vector pCF

<400> 80

ctgttgggct	cgcggttgag	gacaaactct	tcgcggtctt	tccagtactc	ttggatcgga	60
aaccgcgcg	cctccgaacg	gtactccgcc	accgagggac	ctgagcgagt	ccgcatcgac	120
cggatcgga	aacctctcga	ctgttgggg	gagtactccc	tctcaaaagc	gggcatgact	180
tctgcgctaa	gattgtcagt	ttccaaaaac	gaggaggatt	tgatattcac	ctggcccgcg	240
gtgatgcctt	tgagggtggc	cgcgctccatc	tggtcagaaa	agacaatctt	tttgttgtca	300
agcttgagg	gtggcaggct	tgagatctgg	ccatacactt	gagtgacaat	gacatccact	360
ttgcctttct	ctccacaggt	gtccactccc	aggtccaact	gcaggtcgac	tctagaccc	419

<210> 81

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Peptide inhibitor P4-P4' XD-V

<221> MOD\_RES

<222> 4

<223> Xaa is hydroxyethylene or statine

<400> 81

Glu Val Met Xaa Val Ala Glu Phe

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5

<210> 82

<211> 9

<212> PRT

<213> Homo sapiens

<220>

<223> APP fragment P5-P4' wt

<400> 82

Ser Glu Val Lys Met Asp Ala Glu Phe

1

5

<210> 83

<211> 9

<212> PRT

<213> Homo sapiens

<220>

<223> APP fragment P5-P4'wt

<400> 83

Ser Glu Val Asn Leu Asp Ala Glu Phe

1

5

<210> 84

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> APP fragment

<400> 84

Ser Glu Val Lys Leu Asp Ala Glu Phe

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<210> 85

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> APP fragment

<400> 85

Ser Glu Val Lys Phe Asp Ala Glu Phe

1

5

<210> 86

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> APP fragment

<400> 86

Ser Glu Val Asn Phe Asp Ala Glu Phe

1 5

<210> 87

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> APP fragment

<400> 87

Ser Glu Val Lys Met Ala Ala Glu Phe

1 5

<210> 88

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> APP fragment

<400> 88

Ser Glu Val Asn Leu Ala Ala Glu Phe

1 5

<210> 89

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> APP fragment

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Ser Glu Val Lys Leu Ala Ala Glu Phe

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<210> 90

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> APP fragment

<400> 90

Ser Glu Val Lys Met Leu Ala Glu Phe

1

5

<210> 91

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> APP fragment

<400> 91

Ser Glu Val Asn Leu Leu Ala Glu Phe

1

5

<210> 92

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> APP fragment

<400> 92

Ser Glu Val Lys Leu Leu Ala Glu Phe

1

5

<210> 93

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> APP fragment

<400> 93

Ser Glu Val Lys Phe Ala Ala Glu Phe

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<210> 94

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> APP fragment

<400> 94

Ser Glu Val Asn Phe Ala Ala Glu Phe

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<210> 95

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> APP fragment

<400> 95

Ser Glu Val Lys Phe Leu Ala Glu Phe

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<210> 96

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> APP fragment

<400> 96

Ser Glu Val Asn Phe Leu Ala Glu Phe

1

5

<210> 97

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> APP-derived fragment P10-P4' (D-V)

<400> 97

Lys Thr Glu Glu Ile Ser Glu Val Asn Leu Val Ala Glu Phe

1

5

10

<210> 98

<211> 35

<212> DNA

<213> Homo sapiens

<400> 98

cccgaggagc ccggccggag gggcagcttt gtcga

35

<210> 99

<211> 11

<212> PRT

<213> Homo sapiens

<400> 99

Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg

1

5

10

<210> 100

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Recombinant 293T cells

<400> 100

Thr Gln His Gly Ile Arg Leu Pro Leu Arg

1

5

10

<210> 101

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Recombinant 293T cells

<400> 101

Met Val Asp Asn Leu Arg Gly Lys Ser

1

5

<210> 102

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Recombinant CosA2 cells

<400> 102

Gly Ser Phe Val Glu Met Val Asp Asn Leu

1

5

10